

WHAT IS CLAIMED IS:

1. A method of removing a metal from a metal-containing
5 liquid mixture, comprising contacting said liquid
mixture with a solid extractant having a metal-
binding functionality, said metal-binding
functionality comprising an unsubstituted or
substituted phosphine group, said metal-binding
10 functionality being connected to said solid
extractant directly or via a linking moiety which
does not include at least one of a hydrocarbylsilyl
residue or a polyamine residue.
- 15 2. The process of claim 1, wherein said metal comprises
a soft acid.
3. The process of claim 1, wherein said metal comprises
palladium.
- 20 4. The process of claim 1, wherein said metal-binding
functionality comprises triphenyl phosphine.
5. The process of claim 1, wherein said solid
25 extractant comprises a polymer resin.
6. The process of claim 1, wherein said solid
extractant comprises a polystyrene resin and said
metal-binding functionality comprises triphenyl
30 phosphine.
7. The process of claim 1, wherein said liquid mixture
comprises a liquid selected from the group

consisting of tetrahydrofuran, dioxane, acetone,
water, acetic acid, methanol, ethanol, isopropyl
alcohol, 1-butanol, 2-methoxyethanol,
dichloromethane, chloroform, acetonitrile, benzene,
5 toluene, xylenes, mesitylene, anisole, dimethyl
formamide, hexamethylphosphoric triamide, dimethyl
sulfoxide, N,N-dimethyl acetamide, diethyl ether,
methyl t-butyl ether, diisopropyl ether, 1,2-
dimethoxyethane, 1,2-dimethoxypropane, bis(2-
10 methoxyethyl) ether, ethyl acetate, isopropyl
acetate, ethyl propionate, ethyl vinyl ketone,
butanone, hexanes, heptanes, octanes, cyclohexane,
and mixtures thereof.

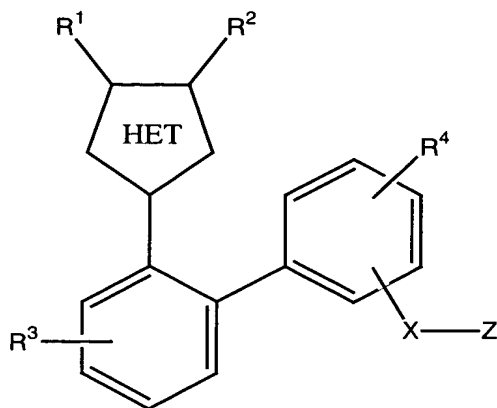
15 8. The process of claim 1, wherein said liquid mixture
comprises a drug substance, or a precursor,
intermediate, salt, solvate, or stereoisomer of a
drug substance.

20 9. A method of recovering a drug substance from a
liquid medium containing said drug substance
together with at least one metal, said method
comprising
25 contacting the liquid medium with a solid
extractant having a metal-binding
functionality, said metal-binding functionality
comprising an unsubstituted or substituted
phosphine group, said metal-binding
functionality being connected to said solid
30 extractant directly or via a linking moiety
which does not include at least one of a
hydrocarbylsilyl residue or a polyamine
residue; and

separating said drug substance from said liquid medium.

10. The method of claim 9, further comprising removing
5 said solid extractant from said liquid medium.

11. The method of claim 9, wherein said drug substance comprises a compound of formula I



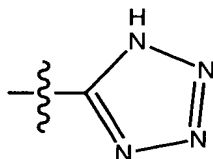
10

(I)

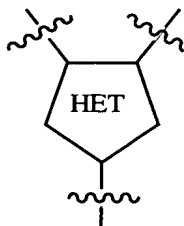
or a salt, solvate, stereoisomer, precursor, prodrug ester, or intermediate thereof, wherein R¹ and R² are the same or different and are independently selected from the group consisting of H, substituted or
15 unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclo, and substituted or unsubstituted aralkyl;
R³ is selected from the group consisting of hydrogen,
20 halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted heterocyclo, substituted or unsubstituted cycloalkyl, substituted or unsubstituted alkylcarbonyl, polyhaloalkyl, cyano, nitro,
25 hydroxy, substituted or unsubstituted amino, substituted

or unsubstituted alkanoyl, substituted or unsubstituted
alkylthio, substituted or unsubstituted alkylsulfonyl,
substituted or unsubstituted alkoxycarbonyl, substituted
or unsubstituted alkylaminocarbonyl, substituted or
5 unsubstituted alkylcarbonylamino, substituted or
unsubstituted alkylcarbonyloxy, and substituted or
unsubstituted alkylaminosulfonyl;
R⁴ is selected from hydrogen, halogen, substituted or
unsubstituted alkyl, substituted or unsubstituted
10 alkenyl, substituted or unsubstituted alkynyl,
substituted or unsubstituted alkoxy, substituted or
unsubstituted aryl, substituted or unsubstituted
heterocyclo, substituted or unsubstituted aralkyl,
substituted or unsubstituted arylalkenyl, substituted or
15 unsubstituted arylalkynyl, substituted or unsubstituted
cycloalkyl, substituted or unsubstituted alkylcarbonyl,
substituted or unsubstituted arylcarbonyl, polyhaloalkyl,
cyano, nitro, hydroxy, substituted or unsubstituted
amino, substituted or unsubstituted alkanoyl, substituted
20 or unsubstituted aroyl, substituted or unsubstituted
alkylthio, substituted or unsubstituted alkylsulfonyl,
substituted or unsubstituted arylsulfonyl, substituted or
unsubstituted alkoxycarbonyl, substituted or
unsubstituted aryloxycarbonyl, substituted or
25 unsubstituted alkylaminocarbonyl, substituted or
unsubstituted arylaminocarbonyl, substituted or
unsubstituted alkylcarbonylamino, substituted or
unsubstituted alkylcarbonyloxy, substituted or
unsubstituted alkylaminosulfonyl, and substituted or
30 unsubstituted arylaminosulfonyl;
R¹, R², R³ and R⁴ may optionally be substituted with up to
5 substituents selected from the group consisting of
hydrogen, halo, alkyl, polyhaloalkyl, alkoxy,

polyhaloalkoxy, alkenyl, alkynyl, cycloalkyl, aryl,
heterocyclo, aralkyl, arylalkenyl, arylalkynyl, aryloxy,
arylazo, hydroxy, nitro, cyano, amino, substituted amino,
thiol, alkylthio, arylthio, heterocyclothio,
5 alkylcarbonyl, arylcarbonyl, acyl, arylaminocarbonyl,
alkoxycarbonyl, aminocarbonyl, alkynylaminocarbonyl,
alkylaminocarbonyl, alkenylaminocarbonyl,
alkylcarbonyloxy, arylcarbonyloxy, alkylcarbonylamino,
arylcarbonylamino, alkoxycarbonylamino, arylsulfinyl,
10 arylsulfinylalkyl, arylsulfonyl, alkylsulfonyl,
aminosulfinyl, aminosulfonyl, arylsulfonylamino,
heterocyclocarbonylamino, heterocyclosulfinyl,
heterocyclosulfonyl, alkylsulfinyl, sulfonamido and
sulfonyl;
15 X represents a valence bond or a divalent linking moiety
which can be read from left to right or vice versa and is
selected from $(CH_2)_n$, $O(CH_2)_n$, $S(CH_2)_n$, cycloalkylene,
 $N(R^5)(CH_2)_n$, $NHCO$, or ethenyl, where n is an integer from
0 to 5, inclusive, and R^5 is hydrogen, alkyl, or alkanoyl;
20 Z is COOR or a tetrazole of the formula

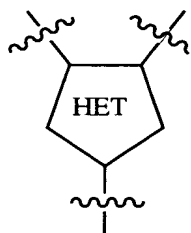


or its tautomer;
wherein R represents a radical selected from the group
consisting of H, alkyl, aryl, aralkyl, cycloalkyl,
heterocyclo, alkenyl, and alkynyl; and
25 the group

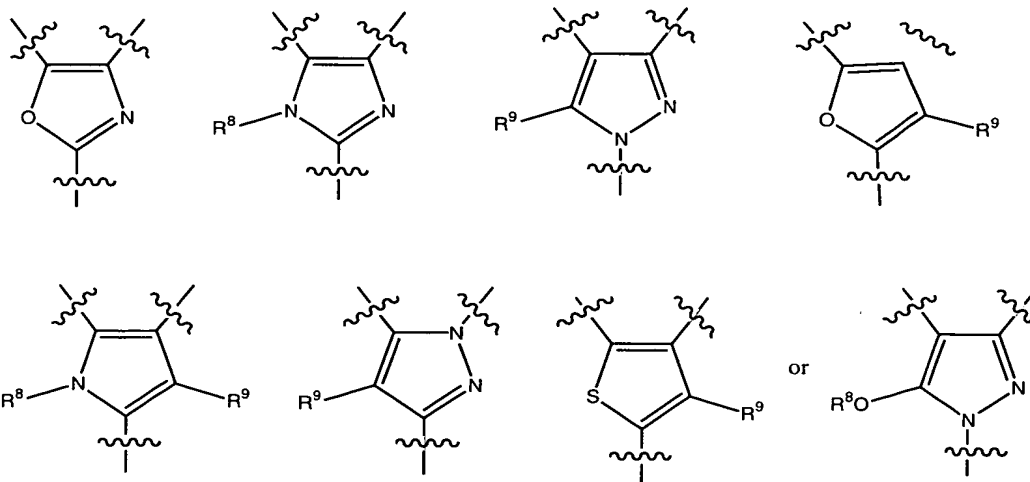


represents a heterocyclo group which may optionally be substituted with one or two substituents which are independently selected from the group consisting of alkyl, alkenyl, oxo, carboxyalkyl, carboxy, cycloalkyl, alkoxy, formyl, alkanoyl, and alkoxy carbonyl, including all stereoisomers thereof.

12. The process of claim 11, wherein, in formula I,



represents



10

wherein

R^8 is hydrogen, alkyl, fluoroalkyl or alkoxyalkyl; and R^9 is hydrogen, alkyl, fluoroalkyl, alkoxy or hydroxyalkyl;

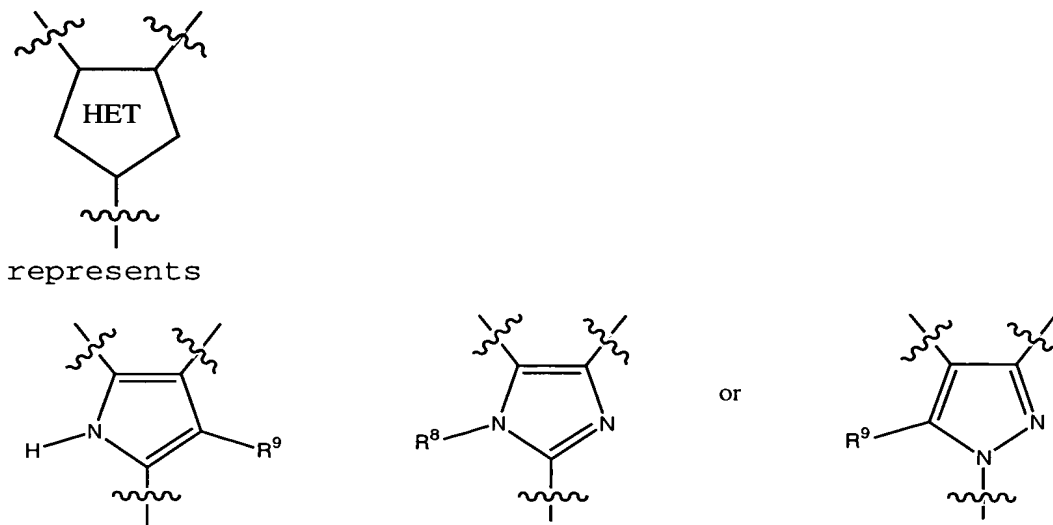
15 and wherein R^1 and R^2 are each phenyl, substituted phenyl or cycloalkyl;

R^3 and R^4 are the same or different and are independently selected from H, halo, alkyl or alkoxy;

X is OCH₂, NHCH₂, CH₂ or CH₂CH₂; and
 Z is CO₂H or tetrazole.

5

13. The process of claim 11, wherein, in formula I,



wherein R⁸ is hydrogen, alkyl or fluoroalkyl;
 10 R⁹ is hydrogen, alkyl, fluoroalkyl or alkoxy; and
 wherein R¹ and R² are each phenyl;
 R³ and R⁴ are each hydrogen;
 X is OCH₂, CH₂ or NHCH₂; and
 Z is CO₂H or tetrazole.

15

14. The process of claim 11, wherein said compound of
 formula I comprises 2'-(5-ethyl-3,4-diphenyl-1H-
 pyrazol-1-yl)-[1,1']-biphenyl-3- yloxyacetic acid.

20 15. The process of claim 11, wherein said metal
 comprises a soft acid.

16. The process of claim 11, wherein said metal comprises palladium.
17. The process of claim 11, wherein said solid
5 extractant comprises a polymer resin.
18. The process of claim 11, wherein said solid extractant comprises a polystyrene resin and said metal binding functionality comprises triphenyl
10 phosphine.
19. A method of recovering a drug substance comprising 2'-(5-ethyl-3,4-diphenyl-1*H*-pyrazol-1-yl)-[1,1']-biphenyl-3-yloxyacetic acid, or a salt, solvate,
15 stereoisomer, precursor, prodrug ester, or intermediate thereof, from a liquid medium containing said drug substance together with at least one metal, said method comprising
20 contacting the liquid medium with a solid extractant having a metal-binding functionality, said metal-binding functionality comprising an unsubstituted or substituted phosphine group, said metal-binding
25 functionality being connected to said solid extractant directly or via a linking moiety which does not include at least one of a hydrocarbylsilyl residue or a polyamine residue; and
30 separating said drug substance from said liquid medium.
20. The method of claim 19, further comprising removing said solid extractant from said liquid medium.

21. The process of claim 19, wherein said metal
comprises a soft acid.
22. The process of claim 19, wherein said metal
5 comprises palladium.
23. The process of claim 19, wherein said solid
extractant comprises a polystyrene resin and said
metal binding functionality comprises triphenyl
10 phosphine.
24. The process of claim 19, wherein said triphenyl
phosphine comprises about 0.1 to about 10 mmol per
gram of the solid extractant.
- 15 25. The process of claim 19, wherein said PPh_3 comprises
about 0.5 to about 3.5 mmol of the solid extractant.
26. The process of claim 19, wherein the solid
20 extractant is present at about 0.01 to about 10% of
the weight of the liquid medium.
27. The process of claim 19, wherein the solid
extractant is present at a weight of about 1 to
25 about 4% of the weight of the liquid medium.
28. The process of claim 19, wherein the liquid medium
is contacted with the solid extractant at a
temperature of about -20° to about 100°C .
- 30 29. The process of claim 19, wherein the liquid medium
is contacted with the solid extractant at a
temperature of about 20° to about 60°C .